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IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

IN RE APPLICATION OF:	)	
Stefan Schorling	) EXAMINER:	David C. Thomas
SERIAL NO.: 10/587,386	) ART UNIT:	1637
FILED: May 3, 2007	) Confirmation No. 4893	
FOR: **NEW PRIMERS AND PROBES FOR THE DETECTION OF PARVOVIRUS B19**	) Attorney Docket No. 22398-US	

PRE-APPEAL BRIEF REQUEST FOR REVIEW

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Applicants have filed a Notice of Appeal of the decision dated December 23, 2010, finally rejecting Claims 4-10, 15 and 16 of the present application. Applicants hereby request a pre-appeal review of the arguments set forth below. This request is being filed together with the Notice of Appeal, which includes a request for a 1-month extension of time to respond to the Final Office Action.

The following documents from the application file are cited in this submission:

- Final Office Action mailed on December 23, 2010 ("Final Action"),
- Applicant's Request for Continued Examination filed March 4, 2010 ("RCE").

General reference is made to Applicant's "prior responses" which includes Applicant's response to the Non-Final Office Action filed on October 7, 2010, and all other responses previously presented.

THE PRESENT INVENTION

The currently pending claims comprise a method for the detection of a target nucleic acid sequence of parvovirus B19 in a sample, comprising: a pair of primers consisting of SEQ ID NO: 15 and SEQ ID NO: 17, amplifying the target nucleic acid, contacting the sample with a probe consisting of SEQ ID NO: 11, and detecting the binding product between the target nucleic acid and the probe as an indication of the presence of the target nucleic acid.

THE REJECTION

The Examiner has maintained the rejections of claim 4 and its dependents under 35 U.S.C. §103(a) as being unpatentable over Schmidt and/or Harder, in view of Hemauer, and further in view of Lowe, Andrus and/or Mosquera. (Final Action pages 2, 6, 11 and 12)

The Examiner asserts, in part, that one of ordinary skill in the art would have been motivated to modify the method of Schmidt along with the cited art to use primers of SEQ ID NOS: 15 and 17 and a probe sequence of SEQ ID NO: 11. Further, the Examiner asserts that the skilled artisan would have had a reasonable expectation of success in modifying the method of Schmidt to substitute for similar and equivalent primers and a probe derived from the same well-known and amplifiable conserved stretch of the NCS-1 region, resulting in the predictable amplification and detection of multiple different parvovirus sequence variants. The Examiner asserts that the claimed primers and probe simply represent structural homologs, or "equivalents", which are derived from sequences suggested by the prior art, and that the claimed primers are *prima facie* obvious over the cited references in the absence of secondary considerations.

THE HISTORY OF APPLICANTS ARGUMENTS

Applicants have argued that none of the cited references alone or in combination teach the specific sequences SEQ ID NOS: 15, 17 and 11, or the combination of these sequences, as provided in the pending claims. Applicants have provided:

1. there was no motivation for one skilled in the art to modify Schmidt in view of Hemauer or Harder to achieve this specific combination of oligos as claimed, and in fact Hemauer teaches away from designing primers in this region,
2. the Examiner has over-generalized the terms "homologs" and/or "equivalents" in the present context of nucleic acid amplification,
3. the selection of the claimed sequences was not "obvious to try", nor was there a reasonable expectation of success as provided by Lowe.

THE *PRIMA FACIE* CASE OF OBVIOUSNESS HAS NOT BEEN ESTABLISHED

1. Schmidt, Hemauer and Harder

The Examiner asserts that Schmidt, Hemauer and Harder teach PCR primers to amplify the NS1 region of parvovirus B19, noting that "additional optimization may be required ... which may require trying other primers". (Final Action page 15) As presented in Applicant's prior responses, one of ordinary skill would NOT have been motivated to modify the method of Schmidt simply because of the fact that others also amplify areas of the NS1 region. This region spans > 2KB which offers thousands of possible alternative oligo sequence design options. There is no motivation provided in either Schmidt, Hemauer or Harder to make primers in different locations of the NS gene other than the specific locations presented in their publications; neither Schmidt nor Hemauer nor Harder discuss the need to improve or change the sequences provided. In fact Hemauer teaches the amplification of 4 distinct regions of the genome, not just NS, and does not provide evidence that one particular region should be selected away from the other 3 to detect parvovirus. Hemauer teaches that many of these regions are more highly conserved than the region targeted by Schmidt, essentially "teaching away" from designing new oligos in the region used by Schmidt. Applicants assert that it is unreasonable to design and test every oligonucleotide possible in a >2kb region, without direction to do so, to achieve the claimed sequences.

2. Homologs and Equivalents

The Examiner asserts that the use of "structural homologs" means that equivalency has been recognized in the prior art since SEQ ID NOs 11, 15 and 17 are homologous to sequences taught by Hemauer. (Final Action page 16) As detailed in prior responses, Applicants assert that the claimed oligos and those taught by the cited art are not "homologous". Applicant's table on page 6 of the RCE summarizes the claimed oligos in comparison to the oligos most closely related as taught by Schmidt and Hemauer. At best, Schmidt provides oligo TP1 which overlaps SEQ ID NO:15 by 5 bases (25%); all other oligos, including those of Harder, have 0% match and are located 22-400, or 2000+ bases away. Different oligo sequences that bind throughout the >2KB region are definitely NOT "equivalents". The Examiner has over-generalized the concept of homologs and equivalents in the context of nucleic acid sequences.

3. Obvious to try

The Examiner asserts that the present invention was "obvious to try" based on the fact that Schmidt teaches oligos within 23 bases of the claimed oligos, and the fact that Hemauer teaches the sequence of the region. (Final Action page 17) As detailed above and in prior responses, none of the cited prior art provides specific direction to design alternative oligos or direction as to which of many possible choices of oligonucleotide design is likely to be successful in the methods as presently claimed. Hemauer teaches a broad range of sequences in the >2KB NS1 gene, many of which are more highly conserved than the region targeted by Schmidt, essentially "teaching away" from designing new oligos in the region used by Schmidt. There are no problems or technical hurdles provided in Schmidt left to be solved ("...the assay is highly reproducible..." Schmidt p. 230 top right column) that would have motivated one skilled in the art to alter the oligos in Schmidt to arrive at the presently claimed invention.

The Federal Circuit (*Kubin* 561 F.3d 1359) has "outlined two classes of situations where 'obvious to try' is erroneously equated with obviousness under § 103." The first situation is applicable here, wherein the invention is not obvious under 103 when:

> "...to vary all parameters or try each of numerous possible choices until one possibly arrived at a successful results, where the prior art gave either no indication of which parameters were critical or no direction as to which of many possible choices is likely to be successful", (*O'Farrell*, 853 F.2d 894).

It was not obvious to select SEQ ID NOS: 15, 17 and 11 or the combination thereof from the large number of possible oligonucleotides and combinations from the parvovirus genome. In the absence of specific direction from the prior art, it was not "obvious to try" the claimed sequences. The "obvious to try" standard is not applicable in this case.

Further, the Examiner asserts that the teachings of Lowe provide guidance for designing primers; in combination with the cited art, one of skill will have a reasonable expectation of success in amplification of the NS1 region using equivalents of the claimed primers. Applicants repeat the assertions above including the Examiner's incorrect use of "equivalents" in the context of nucleic acid sequences, and to the lack of teaching and motivation in the cited art in selecting the particular region of the >2KB area in which to design oligos to achieve the claimed SEQ ID NOS: 15, 17 and 11 of the invention.

CONCLUSION

Applicants assert that the Examiner has not established a *prima facie* case of obviousness. Accordingly, the rejections of claim 4 and its dependents under 35 U.S.C. §103(a) should be withdrawn. The Commissioner is hereby authorized to charge any required fees to Deposit Account No. 50-0812.

Respectfully submitted,

Date: April 25, 2011

By: _____
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